

20. (Amended) The plant of claim 19 wherein said targeting sequence comprises a vacuole-targeting sequence.

22. (Amended) A transgenic seed obtained from the plant of claim 6.

23. (Amended) A transgenic seed obtained from the plant of claim 7 wherein the seed comprises said nucleic acid.

Please add the following new Claim 30:

30. (New) The plant of claim 13, wherein said microorganism is a bacterium or a fungus.

### **REMARKS**

In the above-referenced Office Action, the Examiner rejected Claims 6-9 and 11-23 and withdrew Claims 24-29 from consideration as being drawn to a non-elected invention. This Response cancels Claims 11 and 24-29 without prejudice to, or disclaimer of, the subject matter of these claims; amends Claims 6, 7, 9, 12-15, 18-20, and 22-23; and adds Claim 30. After entry of the foregoing amendments, Claims 6-9, 12-23, and 30 (1 independent claim, 16 total claims) remain pending in the application. Reconsideration is respectfully requested.

### **Objections to the Specification**

The Examiner objects to the specification on various grounds. The Examiner states that the application fails to comply with the requirements of 37 C.F.R. §§ 1.821 through 1.825, as sequence identifiers are missing from the adaptors on pages 26 and 32 and from the primers on pages 39-41 and 46. Applicants submit that, as amended herein, the application is in full compliance with the sequence rules. The specification is amended herein to add sequence identifiers to the adaptors on pages 26 and 32 and to the primers on pages 39-41 and 46. Additionally, sequence identifiers have been added to the consensus translation initiators on page 17 as well as the sequences indicated on page 53.

The Examiner next objects to the drawings for reasons that were supposed to be indicated on an accompanying PTO Form 948. The Examiner indicates that corrected drawings are required and that this objection will not be held in abeyance. However, as the undersigned discussed in a phone conversation with the Examiner, Applicants are not in receipt of PTO Form 948 and, therefore, are unable to respond to this objection. Applicants respectfully request clarification from the Examiner.

The Examiner next objects to the title as not being descriptive of the claimed invention and indicates that a new title is required. Applicants respectfully submit that the title, as amended herein, describes the claimed invention.

The Examiner next objects to the Abstract as not being descriptive of the claimed invention. Applicants enclose a new abstract herewith and respectfully submit that the abstract describes the claimed invention.

The Examiner also indicates that Applicants have not complied with the conditions for receiving the benefit of an earlier filing date under 35 U.S.C. §§ 119(e) and 120 in that the application must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 C.F.R. § 1.78 (a)(2) and (a)(5)). Applicants respectfully submit that the specification is amended herein to include the required reference to the prior applications.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the objections to the specification.

#### **Rejections under 35 U.S.C. § 101**

Claims 6, 11, 18, and 21-22 stand rejected under 35 U.S.C. § 101 because the claimed invention is allegedly directed to non-statutory subject matter. The Examiner contends that the claims are drawn to plants expressing a cellulase and to seeds, which are products of nature. The Examiner suggests that the claims be modified to refer to the hand of the inventor, such as by indicating that the plants and seeds are transformed with a nucleic acid encoding the cellulase. Applicants respectfully traverse this rejection.

Applicants submit that Claims 6, 22, and 23 are amended herein in accordance with the Examiner's suggestion. That is, Claim 6 is amended to recite "A transgenic plant comprising a nucleic acid encoding a cellulase," and Claims 22 and 23 are each amended to recite "A transgenic seed." Since Claim 11 is cancelled herein, this rejection is rendered moot as to that claim. Additionally, since Claims 18 and 21 each depend from Claim 6, the amendment to Claim 6 obviates the rejection as to Claims 18 and 21. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 101.

**Rejections under 35 U.S.C. § 112, ¶ 1: Written Description**

Claims 6-9, 11-14, and 16-23 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors were in possession of the claimed invention at the time the application was filed. Applicants respectfully traverse this rejection.

Applicants submit that the instant specification adequately describes the claimed invention and clearly allows persons of ordinary skill in the art to recognize that Applicants invented the claimed subject matter. As stated in MPEP § 2163.II.A, "[t]he examiner has the initial burden ... of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims." Mere conclusory statements cannot satisfy this burden. Applicants respectfully submit that the Examiner has offered insufficient reasons as to why a person skilled in the art would not recognize that the written description of the invention provides support for the claims.

The Examiner states,

The claims are broadly drawn to a multitude of plants expressing cellulases or transformed with DNA molecules that encode cellulases. In contrast, the specification only describes *Thermomonospora fusca* sequences that encode three  $\beta$ -1,4-endoglucanases [sic]. The specification does not describe all the other DNA molecules encoding cellulases, as encompassed by the claims, and the structural features

that distinguish all such nucleic acids from other nucleic acids are not provided.

Office Action, p. 5.

Contrary to the position advanced by the Examiner, Applicants submit that § 112, first paragraph does not require a description of all other DNA molecules encoding cellulases encompassed by the claims. Nor does it require a description of the structural features that distinguish all such nucleic acids from other nucleic acids. At most, the law requires a description of a representative number of species.

The claimed invention is directed to "[a] transgenic plant comprising a nucleic acid encoding a cellulase" and a transgenic seed obtained therefrom, not to "a nucleic acid encoding a cellulase" *per se*. Therefore, the written description needs to be specific enough to lead the skilled artisan to the class of DNA molecules that encode cellulases. *In re Herschler*, 591 F.2d 693, 702 ("claims drawn to the use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds.") Moreover, as the Office has indicated, a proper determination of whether the written description requirement is satisfied necessitates a reading of the disclosure in the light of the knowledge possessed by those of skill in the art at the time of filing. MPEP § 2163 II.A.2.

Applicants submit that the specification more than satisfies the written description requirements of § 112, first paragraph. For example, the specification teaches *T. fusca* E1, E2, E4, and E5 genes. Specifically, the specification states,

The *T. fusca* genes that encode cellulose-degrading enzymes have been cloned and extensively characterized. (*See, e.g., Collmer et al.* (1983) *Bio/Technology* 1:594-601, hereby incorporated by reference; *Ghangas et al.* (1988) *Appl. Environ. Microbiol.* 54:2521-2526, hereby incorporated by reference; and *Wilson* (1992) *Crit. Rev. Biotechnol.* 12:45-63, hereby incorporated by reference). In addition, the DNA sequences of a cellobiohydrolase gene and an endoglucanase gene from *T. fusca* have been determined (*Jung et al.* (1993) *Appl. Environ. Microbiol.* 59:3032-3043, hereby incorporated by reference); and the DNA sequences of three endoglucanase genes from *T. fusca* have also

been determined (Lao *et al.* (1991) J. Bacteriol. 173:3397-3407, hereby incorporated by reference)....

Specification, p. 4, ¶ 1.

A variety of exemplary genes are taught in the specification, including, for example, a *B. subtilis* endoglucanase and a *C. fimi*  $\beta$ -D-glucosidase (Yoo *et al.* (1992) Biotechnol. Lett. 14:77-82) as well as several cellulases that have been expressed from heterologous systems and have been reported in the literature (see Thomas *et al.*, "Initial Approaches to Artificial Cellulase Systems for Conversion of Biomass to Ethanol" in *Enzymatic Degradation of Insoluble Carbohydrates*, J.N. Saddler and M.H. Penner, eds., ACS Symposium Series 618:208-36, 1995, American Chemical Society, Washington, D.C., Table II, pp. 214-216 (enclosed herewith as Exhibit A). As described in the specification, these exemplary cellulases include, but are not limited to, endoglucanases, exoglucanases, and  $\beta$ -D-glucosidases derived from microorganisms such as bacteria and fungi. See Specification, paragraph bridging pp. 14 and 15.

In addition, the specification provides examples that describe, in detail, plants that express *T. fusca* sequences encoding two  $\beta$ -1,4-endoglucanases (*i.e.*, *T. fusca* E1 and E5) as well as a cellobiohydrolase (*i.e.*, *T. fusca* E2). See Specification at, *inter alia*, pp. 39-45 (Examples A1 through A11).

In view of the foregoing, Applicants submit that the specification reasonably conveys that Applicants were in possession of the claimed invention at the time the application was filed. Not only does the specification provide sufficient teaching to clearly lead the skilled artisan to the relevant class of nucleic acids (*i.e.*, those encoding cellulases) to be transformed into a plant in accordance with the claimed invention, but it more than adequately describes a representative number of species within that class (*i.e.*, DNA molecules encoding: endocellulases, such as  $\beta$ -1,4-endoglucanases; exocellulases, such as cellobiohydrolases; and cellobioses, such as 1,4-  $\beta$ -D-glucosidases).

The Examiner alleges that

Applicant has not described plants expressing cellulases or transformed with DNA molecules that encode cellulases within the full scope of the

claims.... Therefore, *given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions*, it is not clear that Applicant was in possession of the genus claimed at the time the application was filed.

Office Action, p. 5 (emphasis added). In support of these allegations, the Examiner cites *University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), and *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd*, 927 F.2d 1200 (Fed. Cir. 1991).

Applicants respectfully submit the Examiner appears to be incorrectly basing the instant rejection on grounds related to putative "claimed compositions," rather than the claimed transgenic plants and seeds. This is further highlighted by the cases cited by the Examiner, both of which involve claims directed to compositions (*i.e.*, DNA encoding human proinsulin in *Eli Lilly* and DNA encoding human erythropoietin in *Amgen*).

Applicants respectfully submit that the Examiner's reliance on *Eli Lilly* is misplaced. In *Eli Lilly*, the court addresses what is required to sufficiently describe an unknown cDNA molecule that is claimed *per se*. As previously mentioned, in the instant application, the recited nucleic acids encoding cellulases are a known class of molecules and are not claimed *per se*.

The Examiner cites *Amgen* for its statements concerning what is required for the reduction to practice of a gene. However, as previously stated, Applicants are not claiming a gene. Furthermore, the quoted passage from *Amgen* concerns the requirements for reduction to practice in relation to an assessment of prior inventorship under 35 U.S.C. § 102(g), not written description under § 112, first paragraph, which is the basis for the instant rejection. Thus, reliance on *Amgen* is also inappropriate here, since the case addresses the enablement requirement, not the written description requirement. It is well settled that the written description requirement is distinct from the enablement requirement and that there are separate standards for applying each of these provisions of § 112, first paragraph. See, *e.g.*, *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1561 (Fed. Cir. 1991).

For the reasons set forth above, Applicants submit that the instant application provides sufficient written description support for the claimed invention, *i.e.*, a

transgenic plant comprising a nucleic acid encoding a cellulase and a transgenic seed obtained therefrom. The law requires no more. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

**Rejections under 35 U.S.C. § 112, ¶ 1: Enablement**

Claims 6-9, 11-14, and 16-23 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. The Examiner contends that the specification does not reasonably provide enablement for "nucleic acids encoding all cellulases, plants transformed with those cellulases, or non-transformed plants that express cellulases." Office Action, p. 6. The Examiner further contends that the specification does not enable any person skilled in the art to which it pertains to make and use the invention commensurate in scope with these claims. Specifically, the Examiner states that "[t]he instant specification fails to provide guidance for isolation of all cellulase DNAs, and hence for all plants comprising said DNAs." Office Action, p. 6. Applicants respectfully traverse this rejection.

Applicants respectfully submit that the Office has not met its burden of establishing that the practice of the claimed invention would require undue experimentation.

Contrary to the Examiner's allegations, the instant disclosure provides sufficient guidance and direction to enable the practice of the claimed invention without undue experimentation. As discussed above, the specification provides considerable guidance and direction regarding the class of cellulases that may be expressed in a plant in accordance with the claimed invention. In particular, the specification describes various cellulases that have been cloned, characterized, and/or heterologously expressed in bacterial hosts. These described cellulases include endocellulases (*e.g.*,  $\beta$ -1,4-endoglucanases); exocellulases (*e.g.*, cellobiohydrolases); and cellobioses (*e.g.*, 1,4- $\beta$ -D-glucosidases). See, *e.g.*, Specification, p. 4, ¶¶ 1 and 2; and paragraph bridging pp. 14 and 15 (as quoted above).

The Examiner contends that the specification

only provides guidance for expression of constructs comprising a nucleic acid encoding the *T. fusca* E1, E2, or E5  $\beta$ -1,4-endoglucanase operably linked to the tobacco PR-1a or the CaMV 35S promoter in tobacco, maize or wheat (Example A) and similar expression in plants of constructs encoding fusion proteins of those endoglucanases and a vacuolar signal sequence (Example B).

Office Action, p. 6. However, the Examiner fails to set forth sufficient reasons why, in view of the considerable direction and guidance provided by the specification, including, *inter alia*, the noted working examples, the practice of the claimed invention would require undue experimentation.

Applicants respectfully submit that the disclosure provides more than a reasonable amount of guidance and direction for using the disclosed means to express a cellulase in a plant. In addition to providing numerous references that disclose various cellulase genes (see, *e.g.*, Specification, pp. 14-15), the specification provides detailed guidance regarding the modification of microbial genes to optimize nuclear expression of those genes in plants. Specification, pp. 15-18. There is also guidance and direction regarding the construction of plant transformation vectors (Specification, pp. 18-21) as well as the construction of plant expression cassettes (Specification, pp. 21-24), including examples of expression cassette construction and a detailed discussion of various plant expressible promoters that may be employed in the practice of the invention (Specification, pp. 24-33). The specification also provides guidance regarding the transformation of both dicotyledons and monocotyledons (Specification, pp. 33-36), as well as plastid transformation techniques (Specification, pp. 36-38).

Moreover, the specification discloses numerous working examples of various means for expressing cellulase in a plant. There are several examples of the preparation of constructs containing various cellulase coding sequences (*i.e.*, *T. fusca* E1, E2, and E5), each fused either to an inducible or constitutive plant expressible promoter (*i.e.*, tobacco PR-1a or CaMV 35S, respectively) (Examples A1-A6). There are examples of the transformation of various monocot and dicot plants (*i.e.*, tobacco, maize, and wheat) with the disclosed cellulase constructs (Examples A7-A9). There are examples



regarding the vacuole-targeted expression of cellulases (Examples B1-B13). There are also examples of chloroplast expression of cellulase genes (Examples C1-C13).

Applicants respectfully submit that the working examples, in conjunction with the remainder of the disclosure, provide sufficient guidance and direction to enable one skilled in the art to practice the claimed invention employing no more than routine experimentation. Specifically, in view of the advanced state of the transformation art as of the filing date of the instant application and the specification's detailed guidance and direction regarding the transformation of plants to achieve the expression of cellulase, a skilled artisan would have been able to transform a plant with any of a variety of known cellulase genes employing no more than routine experimentation.

The Examiner contends that

[a]s the specification does not describe the transformation of any plant with a gene encoding a cellulase other than the three *T. fusca*  $\beta$ -1,4-endoglucanase [sic], undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those that express cellulase, if such plants are even obtainable.

Office Action, p. 7.

However, the Examiner is reminded that "[e]nablement is not precluded by the necessity for some experimentation such as routine screening." *In re Wands*, 858 F.2d 731, 736-737 (Fed. Cir. 1988). In fact, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.* at 737 (internal citation omitted). The instant specification provides such guidance, via general teachings and more detailed examples. Practicing non-exemplified embodiments of the claimed invention would have required the routine preparation of vector constructs, in accordance with the teachings of the disclosure, and limited and systematic routine screening of, for example, plants transformed to express the various disclosed species within the described genus of cellulase genes. Applicants respectfully submit that, even where required, such efforts do not rise to the level of undue experimentation.

For the foregoing reasons, Applicants respectfully submit that the instant specification, coupled with what was known in the art at the time of filing, would have provided sufficient guidance to enable one of ordinary skill in the art to practice the claimed invention without undue experimentation. Accordingly, the claimed invention is enabled, and Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

**Rejection under 35 U.S.C. § 112, ¶ 2**

Claims 6-9 and 11-23 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Applicants respectfully traverse this rejection.

Regarding Claim 6, the Examiner contends that the term "cellulase" is indefinite because this term is used in the art to refer to a wide variety of cellulose degrading enzymes, and it is not clear which of these is intended.

Applicants respectfully submit that the mere fact that the term cellulase refers to a variety of cellulase degrading enzymes does not render the term indefinite. It is well settled that the breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 693 (C.C.P.A. 1971). Applicants further submit that the term "cellulase," as recited in Claim 6, is amply supported in the specification and is, therefore, not indefinite. For example, the specification states, "[c]ellulases are a family of enzymes that work in concert to break down cellulose to its simple sugar components ..." Specification, p. 2, lines 15-17. The specification further states, "[c]ellulases that may be expressed in plants according to the present invention include, but are not limited to, endoglucanases, exoglucanases, and  $\beta$ -D-glucosidases ..." Specification, p. 6, lines 6-7. Applicants respectfully remind the Examiner that "[t]hey can define in the claims what they regard as their invention essentially in whatever terms they choose so long as the terms are not used in ways that are contrary to accepted meanings in the art." MPEP § 2173.01. Accordingly, the claim term "cellulase" satisfies the notice function of § 112, second paragraph, and clearly informs those of ordinary skill in the art of the metes and

bounds of the claimed invention. Applicants acknowledge the Examiner's position that for the purpose of examination of the instant application cellobiohydrolases and cellobioses "were not considered cellulases for purposes of examination." Office Action, p. 7. Applicants do not agree with this position, since these are indeed cellulases.

The Examiner further states that dependent Claim 11 recites cellobiohydrolases ( $\beta$ -1,4-exoglucanases) and cellobioses (e.g., 1,4-  $\beta$ -D-glucosidases) separately from "cellulases" in the Markush group and that these enzymes were not considered as cellulases for purposes of examination. Claim 11 is cancelled herein, thereby rendering this point moot.

Regarding Claims 11-13, the Examiner states that the claims lack antecedent basis for the phrase "the cellulose-degrading enzyme." Applicants respectfully submit that since Claim 11 is cancelled herein, this rejection is rendered moot as to that claim. Further, Claims 12 and 13 no longer recite "the cellulose-degrading enzyme," thereby obviating the rejection.

The Examiner further states that Claim 11 is not written in proper Markush format. Applicants respectfully submit that since Claim 11 is cancelled herein, this rejection is rendered moot.

The Examiner further contends that the word "preferably" in Claim 13 renders the claim indefinite because it is unclear whether the limitation following the word is part of the claimed invention. Applicants respectfully submit that Claim 13 no longer recites the term "preferably," thereby obviating the rejection.

Regarding Claim 18, the Examiner states that the placement of words within parenthesis renders the claim indefinite because it is unclear whether the limitation following the word is part of the claimed invention. Applicants respectfully submit that Claim 18 no longer recites terms within parenthesis, thereby obviating the rejection.

Regarding Claims 19 and 20, the Examiner states that recitation of the phrase "targeting sequence" is indefinite because it is unclear whether the targeting sequence is

a protein attached to the heterologous DNA or whether a nucleic acid encoding a targeting sequence is further comprised by the heterologous DNA. Applicants respectfully submit that Claim 19 has been amended to recite "wherein said nucleic acid further encodes a targeting sequence," and more particularly points out and distinctly claims the subject matter that Applicants regard as their invention. Since Claim 20 depends from Claim 19, the rejection as to Claim 20 is also obviated.

Regarding Claim 21, the Examiner states that the recitation of the term "thermostable" is unclear because all cellulases are stable at some temperature. Applicants respectfully submit that the term "thermostable" is an art-recognized term. Generally, those skilled in the art would readily appreciate what is encompassed by the term. Thermostable cellulases are known in the art and those skilled in the art readily recognize what is meant by this feature. See, *e.g.*, Collmer *et al.* (1983) *Bio/Technology* 1:594-601, p. 594; and Wilson (1992) *Crit. Rev. Biotechnol.* 12:45-63, p. 45 (enclosed herewith as Exhibits B and C).

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the claim rejections under 35 U.S.C. § 112, second paragraph.

#### **Rejection under 35 U.S.C. § 102: Yoshikawa**

Claims 6-7, 11, and 17-23 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Yoshikawa *et al.* (1993, *Naturwissenschaften* 80:417-420) ("Yoshikawa") in light of each of Takeuchi *et al.* (1990, *Plant Physiol.* 93:673-682) ("Takeuchi") and Melchers *et al.* (1993, *Plant Mol. Biol.* 21:583-593) ("Melchers"). The Examiner contends that Yoshikawa teaches tobacco plants transformed with a nucleic acid encoding a soybean  $\beta$ -1,3-endoglucanase expressed behind the CaMV 35S promoter and seeds produced from those transformed plants, wherein the seeds comprise the nucleic acid (p. 417 and Figure 1). Office Action, p. 9, ¶ 17. The Examiner cites Takeuchi to support the contention that the  $\beta$ -1,3-endoglucanase disclosed in Yoshikawa includes a signal peptide, and Melchers is relied upon to support the contention that the  $\beta$ -1,3-endoglucanase disclosed by Yoshikawa encodes a vacuolar targeting sequence. Applicants respectfully traverse this rejection with respect

to claim 6-7 and 17-23. Since Claim 11 is cancelled herein, this rejection is rendered moot as to that claim.

Applicants respectfully submit that Yoshikawa does not disclose a "transgenic plant comprising a nucleic acid encoding a cellulase" or a transgenic seed obtained therefrom, as recited in Claims 6-7 and 17-23. As the Examiner is no doubt aware, cellulose is a  $\beta$ -1,4-linked polymer of glucose. Cellulases are a class of enzymes that degrade cellulose by hydrolyzing the  $\beta$ -1,4 linkages of cellulose. Applicants submit that the  $\beta$ -1,3-endoglucanase disclosed in Yoshikawa is not a cellulase. As such, Yoshikawa, considered alone or in light of Takeuchi and Melchers, does not teach each and every element of the claimed invention and cannot be said to anticipate the claimed invention.

Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(b).

**Rejection under 35 U.S.C. § 102: Lashbrook**

Claims 6, 11, 18, and 21-22 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Lashbrook *et al.* (1994, Plant Cell 6:1485-1493) ("Lashbrook"). The Examiner contends that Lashbrook teaches that tomato plants express endo- $\beta$ -1,4-glucanase at various times during fruit ripening (Figure 3). Office Action, p. 9, ¶ 18. The Examiner further contends that the fruit would inherently comprise seeds and that the cellulase would be "thermostable." Applicants respectfully traverse this rejection with respect to claims 6, 18, and 21-22. Since Claim 11 is cancelled herein, this rejection is rendered moot as to that claim.

Applicants respectfully submit that Lashbrook does not disclose a "transgenic plant comprising a nucleic acid encoding a cellulase" and a transgenic seed obtained therefrom, as recited in amended Claims 6, 18, and 21-22. For example, the plants disclosed in Lashbrook are not transgenic; that is, Lashbrook discloses endoglucanases that are native to, and expressed in, tomato. Further, the reference itself does not teach that the plants disclosed therein comprise a nucleic acid encoding a cellulase. Quite to

the contrary, the authors acknowledge that “[a]lthough the term ‘cellulase’ has been widely used to describe these endoglucanases, the term is misleading in view of the current lack of evidence for EGase-catalyzed cellulose degradation.” Lashbrook, p. 1486. Further, “the nature of the cell wall substrate(s) modified by these enzymes and thus their physiological function are unknown.” *Id.* Thus, Lashbrook does not disclose each and every element of the claimed invention and cannot be said to anticipate the claimed invention.

Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(b).

#### **Rejection under 35 U.S.C. § 102: Borriss**

Claims 6-7, 11-13, 18, and 21 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Borriss *et al.*, U.S. Patent No. 5,470,725, filed February 16, 1990 (“Borriss”). The Examiner contends that Borriss teaches a nucleic acid encoding a thermostable  $\beta$ -(1,3-1,4)-endoglucanase constructed by hybridizing parts of  $\beta$ -glucanase genes from two different *Bacillus* species (col. 3, lines 11-24). Office Action, pp. 9-10, ¶ 19. Borriss is also said to teach plants transformed with the nucleic acid (claim 55). The Examiner further contends that because the plant is capable of expressing the nucleic acid (see parent claim 41), the nucleic acid would be operably linked to a promoter active in plants. Applicants respectfully traverse this rejection with respect to claims 6-7, 12-13, 18, and 21. Since Claim 11 is cancelled herein, this rejection is rendered moot as to that claim.

Applicants respectfully submit that Borriss does not disclose a “transgenic plant comprising a nucleic acid encoding a cellulase” and a transgenic seed obtained therefrom, as recited in amended Claims 6-7, 12-13, 18, and 21. For example, Borriss does not describe a cellulase. Borriss discloses a (1,3-1,4)- $\beta$ -glucanase and teaches that “(1,3-1,4)-  $\beta$ -glucanases ... cleave the  $\beta$ -glycosidic linkages in (1,3-1,4)-  $\beta$ -glucans.” Col. 1, lines 15-18. Applicants submit that (1,3-1,4)-  $\beta$ -glucans are not components of cellulose. Since (1,3-1,4)-  $\beta$ -glucanases are not cellulases, Borriss does not disclose

each and every element of the claimed invention. Accordingly, Borriss does not anticipate Claims 6-7, 12-13, 18, and 21.

Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(e).

**Rejection under 35 U.S.C. § 102: Ryals**

Claims 6-9, 11-13, and 18-23 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Ryals *et al.*, U.S. Patent No. 5,614,395, filed January 13, 1994 ("Ryals"). The Examiner contends that Ryals teaches plants transformed with nucleic acids encoding  $\beta$ -1,3-endoglucanases wherein the nucleic acid is expressed behind a PR-1a promoter (claims 7-8 and 10). Office Action, p. 10, ¶ 20. The Examiner asserts that the  $\beta$ -1,3-endoglucanase would be thermostable and would inherently comprise a vacuole targeting sequence. The Examiner further contends that Ryals also teaches seeds from plants transformed with a construct comprising a promoter and a  $\beta$ -1,3-endoglucanase sequence, including seed comprising the construct (col. 146, lines 6-25). *Id.* Applicants respectfully traverse this rejection with respect to claims 6-9, 12-13, and 18-23. Since Claim 11 is cancelled herein, this rejection is rendered moot as to that claim.

Applicants respectfully submit that Ryals does not disclose a "transgenic plant comprising a nucleic acid encoding a cellulase" and a transgenic seed obtained therefrom, as recited in amended Claims 6-9, 12-13, and 18-23. In particular, for the reasons stated above with respect to Yoshikawa,  $\beta$ -1,3-endoglucanases are not cellulases. Thus, Ryals does not disclose each and every element of the claimed invention.

Accordingly, Ryals does not anticipate Claims 6-9, 12-13, and 18-23. Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(e).

**Rejection under 35 U.S.C. § 103: Bennett**

Claims 6-8, 11, 16-18, and 21-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bennett *et al.*, U.S. Patent No. 5,168,064, issued December 1, 1992 ("the '064 Patent"). The Examiner contends that the '064 Patent discloses a nucleic acid encoding a tomato endo- $\beta$ -1,4-glucanase and plants transformed with antisense constructs comprising that nucleic acid expressed behind the chemically inducible E8 promoter and the constitutive CaMV 35S promoter (col. 17, line 9 to col. 21, line 49). Office Action, pp. 10-11, ¶ 22. The Examiner further contends that the tomato endo- $\beta$ -1,4-glucanase would be "thermostable." The Examiner acknowledges that the '064 Patent does not disclose plants transformed with the construct in a sense orientation. Nevertheless, the Examiner asserts that it would have been obvious to one of ordinary skill in the art to modify the method of transforming plants with an antisense endo- $\beta$ -1,4-glucanase-encoding construct, as taught by the '064 Patent, to express the endo- $\beta$ -1,4-glucanase in a sense orientation. The Examiner further states that one of ordinary skill in the art would have been motivated to do so at the suggestion of the '064 Patent (col. 3, lines 23-25). *Id.* Applicants respectfully traverse this rejection with respect to claims 6-8, 16-18, and 21-23. Since Claim 11 is cancelled herein, this rejection is rendered moot as to that claim.

Applicants respectfully submit that the Office has not met its burden of establishing a *prima facie* case of obviousness over the '064 Patent. A *prima facie* case of obviousness requires that three criteria be met: (1) there must be some suggestion or motivation to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. See MPEP § 2142.

Applicants note that two of the inventors (*i.e.*, Bennett and Lashbrook) of the '064 Patent are also authors of the later published Lashbrook reference cited by the Examiner and discussed in detail above. Further, the amino acid sequence of the endo- $\beta$ -1,4-glucanase disclosed in Table I of the '064 Patent is the same sequence later identified in Lashbrook as the endo- $\beta$ -1,4-glucanase Cel 1 (see Figure 1). Thus, as



discussed previously, and by the inventors' own admission, the endo- $\beta$ -1,4-glucanase disclosed in the '064 Patent is not a cellulase. As the inventors state, "[a]lthough the term 'cellulase' has been widely used to describe these endoglucanases, the term is misleading in view of the current lack of evidence for EGase-catalyzed cellulose degradation." Lashbrook, p. 1486. Further, "the nature of the cell wall substrate(s) modified by these enzymes [*i.e.*, endoglucanases expressed in tomato plants during fruit ripening] and thus their physiological function are unknown." *Id.* Thus, the reference cited by the Examiner does not teach or suggest all of the claim elements.

For the reasons set forth above, Applicants submit that the '064 Patent does not render Claims 6-8, 16-18, and 21-23 obvious. Accordingly, the claims are patentable over the reference, and Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

**Rejection under 35 U.S.C. § 103: Yoshikawa in view of Lao**

Claims 6-7, 11-15, and 17-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yoshikawa in view of Lao *et al.* (1991, J. Bacteriol. 173:3397-3407) ("Lao"). The Examiner acknowledges that Yoshikawa does not disclose plants transformed with a nucleic acid encoding a *T. fusca*  $\beta$ -1,4-endoglucanase. However, the Examiner contends that Lao teaches genes encoding the *T. fusca* E2 and E5  $\beta$ -1,4-endoglucanases and that it would have been obvious to one of ordinary skill in the art to modify the method of making plants resistant to fungal diseases by transformation with an enzyme that attacks  $\beta$ -glucans, as taught by Yoshikawa, by substituting the  $\beta$ -glucan degrading enzyme (*i.e.*,  $\beta$ -1,4-glucanase) described in Lao. The Examiner further contends that one of ordinary skill in the art would have been motivated to do so because substitution of one  $\beta$ -glucan degrading enzyme for another would be an obvious optimization of experimental parameters. Applicants respectfully traverse this rejection with respect to claims 6-7, 12-15, and 17-23. Since Claim 11 is cancelled herein, this rejection is rendered moot as to that claim.

Applicants respectfully submit that the Office has not met its burden of establishing a *prima facie* case of obviousness over Yoshikawa in view of Lao.

Specifically, Applicants submit that modification of Yoshikawa in the manner proposed by the Examiner would render Yoshikawa's purported invention unsatisfactory for its intended purpose. Therefore, there would have been no motivation to make the proposed modification.

As discussed in detail above, the  $\beta$ -1,3-endoglucanase disclosed in Yoshikawa is not a cellulase. Further, there is no evidence suggesting that the cellulases disclosed in Lao have the same or similar enzymatic activity to Yoshikawa's  $\beta$ -1,3-endoglucanase. Thus, there would have been no motivation for one skilled in the art to modify Yoshikawa's method for rendering plants resistant to fungal diseases by substituting Lao's cellulases for Yoshikawa's  $\beta$ -1,3-endoglucanase because the modification would have rendered the method unsatisfactory for its intended purpose, that is, "the generation of elicitor signals leading to active disease resistance." Yoshikawa, p. 417. Consequently, a *prima facie* case of obviousness has not been established.

For the reasons set forth above, Applicants submit that Yoshikawa in view of Lao does not render Claims 6-7, 12-15, and 17-23 obvious. Accordingly, the claims are patentable over the references cited by the Examiner, and Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

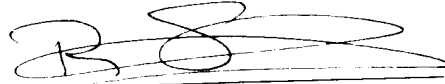
### CONCLUSION

Pursuant to the foregoing remarks, Applicants respectfully submits that all of the pending claims fully comply with 35 U.S.C. § 112 and are allowable over the prior art of record. No new matter is added by this amendment. Reconsideration of the application and allowance of all pending claims is earnestly solicited. Should the Examiner wish to discuss any of the above in greater detail or deem that further amendments should be made to improve the form of the claims, then the Examiner is invited to telephone the undersigned at the Examiner's convenience.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attached marked-up pages are captioned

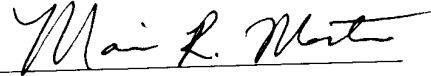
"Version With Markings To Show Changes Made". Entry of the amendments is respectfully requested.

Respectfully submitted,



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**Version With Markings To Show Changes Made**

**In the Specification**

On page 1, the title has been amended as follows:

Transgenic Plants Expressing A Cellulase [Cellulolytic Enzymes]

Page 1 has been amended to add the following below the title:

**CROSS REFERENCE TO RELATED APPLICATIONS**

This application is a divisional of U.S. Application Serial No. 09/254,780, filed March 10, 1999, which is a national stage application under 35 U.S.C. § 371 of International Application No. PCT/US97/16187, filed September 12, 1997, which claims the benefit of U.S. Provisional Application Serial No. 60/054,528, filed August 4, 1997, and U.S. Provisional Application Serial No. 60/025,985, filed September 12, 1996, all of which are herein incorporated by reference in their entireties.

On page 17, the first paragraph has been amended as follows (text that has been added is double-underlined to differentiate it from the originally underlined text):

Plants differ from microorganisms in that their messages do not possess a defined ribosome binding site. Rather, it is believed that ribosomes attach to the 5' end of the message and scan for the first available ATG at which to start translation. Nevertheless, it is believed that there is a preference for certain nucleotides adjacent to the ATG and that expression of microbial genes can be enhanced by the inclusion of a eukaryotic consensus translation initiator at the ATG. Clontech (1993/1994 catalog, page 210) have suggested the sequence GTCGACCATGGTC (SEQ ID NO:1) as a consensus translation initiator for the expression of the *E. coli uidA* gene in plants. Further, Joshi (NAR 15: 6643-6653 (1987)) has compared many plant sequences adjacent to the ATG and suggests the consensus

TAAACAATGGCT (SEQ ID NO:2). In situations where difficulties are encountered in the expression of microbial ORFs in plants, inclusion of one of these sequences at the initiating ATG may improve translation. In such cases the last three nucleotides of the consensus may not be appropriate for inclusion in the modified sequence due to their modification of the second AA residue. Preferred sequences adjacent to the initiating methionine may differ between different plant species. A survey of 14 maize genes located in the GenBank database provided the following results:

On page 26, paragraphs 2 and 3 have been amended as follows:

pCGN1761ENX is cleaved with *SphI*, treated with T4 DNA polymerase and religated, thus destroying the *SphI* site located 5' to the double 35S promoter. This generates vector pCGN1761ENX/*Sph*-. pCGN1761ENX/*Sph*- is cleaved with *EcoRI*, and ligated to an annealed molecular adaptor of the sequence 5'-AATTCTAAAGCATGCCGATCGG-3' (SEQ ID NO:3) / 5'-AATTCCGATCGGCATGCTTTA-3' (SEQ ID NO:4). This generates the vector pCGNSENX which incorporates the *quasi*-optimized plant translational initiation sequence TAAA-C adjacent to the ATG which is itself part of an *SphI* site which is suitable for cloning heterologous genes at their initiating methionine. Downstream of the *SphI* site, the *EcoRI*, *NotI*, and *XhoI* sites are retained.

An alternative vector is constructed which utilizes an *NcoI* site at the initiating ATG. This vector, designated pCGN1761NENX is made by inserting an annealed molecular adaptor of the sequence 5'-AATTCTAAACCATGGCGATCGG-3' (SEQ ID NO:5) / 5'-AATTCCGATCGCCATGGTTTA-3' (SEQ ID NO:6) at the pCGN1761ENX *EcoRI* site. Thus, the vector includes the *quasi*-optimized sequence TAAACC adjacent to the initiating ATG which is

within the *NcoI* site. Downstream sites are *EcoRI*, *NotI*, and *XhoI*. Prior to this manipulation, however, the two *NcoI* sites in the pCGN1761ENX vector (at upstream positions of the 5' 35S promoter unit) are destroyed using similar techniques to those described above for *SphI* or alternatively using "inside-outside" PCR (Innes *et al.* PCR Protocols: A guide to methods and applications. Academic Press, New York (1990). This manipulation can be assayed for any possible detrimental effect on expression by insertion of any plant cDNA or reporter gene sequence into the cloning site followed by routine expression analysis in plants.

On page 32, paragraph 2 has been amended as follows:

A preferred vector is constructed by transferring the *DraI-SphI* transit peptide encoding fragment from prbcS-8B to the cloning vector pCGN1761ENX/Sph-. This plasmid is cleaved with *EcoRI* and the termini rendered blunt by treatment with T4 DNA polymerase. Plasmid prbcS-8B is cleaved with *SphI* and ligated to an annealed molecular adaptor of the sequence 5'-CCAGCTGGAATTCCG-3' (SEQ ID NO:7) / 5'-CGGAATTCCAGCTGGCATG-3' (SEQ ID NO:8). The resultant product is 5'-terminally phosphorylated by treatment with T4 kinase. Subsequent cleavage with *DraI* releases the transit peptide encoding fragment which is ligated into the blunt-end *ex-EcoRI* sites of the modified vector described above. Clones oriented with the 5' end of the insert adjacent to the 3' end of the 35S promoter are identified by sequencing. These clones carry a DNA fusion of the 35S leader sequence to the *rbcS-8A* promoter-transit peptide sequence extending from -58 relative to the *rbcS* ATG to the ATG of the mature protein, and including at that position a unique *SphI* site, and a newly created *EcoRI* site, as well as the existing *NotI* and *XhoI* sites of pCGN1761ENX. This new vector is designated

pCGN1761/CT. DNA sequences are transferred to pCGN1761/CT in frame by amplification using PCR techniques and incorporation of an *SphI*, *NSphI*, or *NlaIII* site at the amplified ATG, which following restriction enzyme cleavage with the appropriate enzyme is ligated into *SphI*-cleaved pCGN1761/CT. To facilitate construction, it may be required to change the second amino acid of cloned gene, however, in almost all cases the use of PCR together with standard site directed mutagenesis will enable the construction of any desired sequence around the cleavage site and first methionine of the mature protein.

On page 39, paragraph 2 has been amended as follows (text that has been added is double-underlined to differentiate it from the originally underlined text):

Example A1: Preparation of a chimeric gene containing the T. fusca E1 cellulase coding sequence fused to the tobacco PR-1a promoter

Plasmid pGFE1 (Jung et al. (1993) Appl. Environ. Microbiol. 59, 3032-3043) containing the T. fusca E1 gene (GenBank accession number L20094), which codes for a protein with endoglucanase activity, was used as the template for PCR with a left-to-right "top strand" primer comprising an ATG before the first codon of the mature E1 protein, the first 21 base pairs of the mature protein and a *NcoI* restriction site at the newly created ATG (primer E11: GCG CCC ATG GAC GAA GTC AAC CAG ATT CGC) (SEQ ID NO:9) and a right-to-left "bottom strand" primer homologous to positions 322 to 346 from the newly created ATG of the E1 gene (primer E12: CCA GTC GAC GTT GGA GGT GAA GAC) (SEQ ID NO:10). This PCR reaction was undertaken with AmpliTaq DNA polymerase according to the manufacturer's recommendations (Perkin Elmer/Roche, Branchburg, NJ) for five cycles at 94°C (30 s), 40°C (60 s), and 72°C (30 s) followed by 25 cycles at 94°C (30 s), 55°C (60 s) and 72°C (30 s). This generated a product of 352 bp containing a *NcoI* site at its left

end and a *EcoRI* site at its right end and comprised the 5' end of the E1 gene without the signal sequence. The fragment was gel purified using standard procedures, cleaved with *NcoI* and *EcoRI* (all restriction enzymes purchased from Promega, Madison, WI or New England Biolabs, Beverly, MA) and ligated into the *NcoI* and *EcoRI* sites of pTC191 (De La Fuente *et al.* (1994) Gene 139, 83-86) to obtain pE1.

The paragraph bridging pages 40 and 41 has been amended as follows (text that has been added is double-underlined to differentiate it from the originally underlined text):

Example A2: Preparation of a chimeric gene containing the *T. fusca* E2 cellulase coding sequence fused to the tobacco PR-1a promoter

Plasmid pJT17 containing the *T. fusca* E2 gene (Ghangas *et al.* (1988) Appl. Environ. Microbiol. 54, 2521-2526; Lao *et al.* (1991) J. Bacteriol. 173, 3397-3407) (GenBank accession number M73321), which codes for a protein with cellobiohydrolase activity, was used as the template for PCR with a left-to-right "top strand" primer comprising an ATG before the last codon of the E2 signal sequence, the first 18 base pairs of the mature protein and a *NcoI* restriction site at the newly created ATG (primer E21: GCG CGC CAT GGC CAA TGA TTC TCC GTT CTA C) (SEQ ID NO:11) right-to-left "bottom strand" primer homologous to positions 310 to 334 from the newly created ATG of the E2 gene (primer E22: GGG ACG GTT CTT CAG TCC GGC AGC) (SEQ ID NO:12). This PCR reaction was undertaken with AmpliTaq DNA polymerase according to the manufacturer's recommendations for five cycles at 94°C (30 s), 40°C (60 s), and 72°C (30 s) followed by 25 cycles at 94°C (30 s), 55°C (60 s) and 72°C (30 s). This generated a product of 341 bp containing a *NcoI* site at its left end and a *EcoRI* site at its right end comprising the 5' end of the E2 gene without a signal sequence. The fragment was gel purified using



standard procedures, cleaved with *NcoI* and *EcoRI* and ligated into the *NcoI* and *EcoRI* sites of pTC191 to obtain pE2.

The paragraph bridging pages 41 and 42 has been amended as follows (text that has been added is double-underlined to differentiate it from the originally underlined text):

Example A3: Preparation of a chimeric gene containing the *T. fusca* E5 cellulase coding sequence fused to the tobacco PR-1a promoter

Plasmid pD374, a modified version of pD370 (Collmer and Wilson (1983) *Biotechnology* 1, 594-601; Lao et al. (1991) *J. Bacteriol.* 173, 3397-3407) containing the *T. fusca* E5 gene (GenBank accession number L01577), which codes for a protein with endoglucanase activity, was used as the template for PCR with a left-to-right "top strand" primer comprising an ATG before the first codon of the mature E5 protein, the first 21 base pairs of the mature protein and a *NcoI* restriction site at the newly created ATG (primer E51: CGC CCA TGG CCG GTC TCA CCG CCA CAG TC) (SEQ ID NO:13) and a right-to-left "bottom strand" primer homologous to positions 89 to 114 from the newly created ATG of the E5 gene (primer E52: GAC GAC CTC CCA CTG GGA GAC GGT G) (SEQ ID NO:14). AmpliTaq DNA polymerase was used for PCR according to the manufacturer's recommendations for five cycles at 94°C (30 s), 40°C (60 s), and 72°C (30 s) followed by 25 cycles at 94°C (30 s), 55°C (60 s) and 72°C (30 s). This generated a product of 119 bp containing a *NcoI* site at its left end and a *XhoI* site at its right end and comprised the 5' end of the E5 gene without a signal sequence. The fragment was gel purified, cleaved with *NcoI* and *XhoI* and ligated into the *NcoI* and *XhoI* sites of pCIB4247 to obtain pCE5. pCIB4247 is a pUC19 derivative (Yanisch-Perron et al. (1985) *Gene* 33, 103-119) containing a polylinker with *NcoI*, *XhoI* and *EcoRI* restriction sites.

The paragraph bridging pages 46 and 47 has been amended as follows (text that has been added is double-underlined to differentiate it from the originally underlined text):

Example B1: Preparation of a chimeric gene containing the *T. fusca* E5 cellulase coding sequence fused to the tobacco PR-1a promoter

Plasmid pD374 containing the *T. fusca* E5 gene (see Example A3) was used as template for PCR with a left-to-right "top strand" primer extending from position 1,135 to 1,156 in the E5 gene relative to the endogenous ATG and comprising an additional *NcoI* site at its left end (primer VAC1: CAT GCC ATG GGT GAG GCC TCC GAG CTG TTC C) (SEQ ID NO:15) and a right-to-left "bottom strand" primer whose sequence was homologous to the 21 last bp of the E5 gene and including 21 bp of a vacuolar targeting sequence derived from a tobacco chitinase gene (Shinshi et al. (1990) Plant Mol. Biol. 14, 357-368, Neuhaus et al. (1991) Proc. Natl. Acad. Sci. USA 88, 10362-10366), the stop codon of the same tobacco chitinase gene and a *SacI* restriction site (primer VAC2: TGC GAG CTC TTA CAT AGT ATC GAC TAA AAG TCC GGA CTG GAG CTT GCT CCG CAC) (SEQ ID NO:16). AmpliTaq DNA polymerase was used for PCR according to the manufacturer's recommendations for five cycles at 94°C (30 s), 40°C (60 s), and 72°C (30 s) followed by 25 cycles at 94°C (30 s), 55°C (60 s) and 72°C (30 s). This generated a product of 283-bp containing the 3' end of the E5 gene fused to the vacuolar targeting sequence. The fragment was gel purified, cleaved with *NcoI* and *SacI* and ligated into the *NcoI* and *SacI* sites of pJG203 to obtain pJGDE5.

The paragraph bridging pages 52 and 53 has been amended as follows (text that has been added is double-underlined to differentiate it from the originally underlined text):

Example C2: Preparation of a modified tobacco plastid transformation vector containing the *T. fusca* E5 cellulase coding sequence fused to a modified bacteriophage T7 gene 10

promoter and terminator engineered for reduced read-through transcription

Plasmid pC8 was digested with *SpeI* and *NcoI* and a 235 bp fragment containing the T7 gene 10 promoter and a portion of the divergent *psbA* gene promoter and 5' UTR was isolated by gel purification and cloned into the *NcoI* and *SpeI* restriction sites of vector pGEM5Zf+ (Promega, Madison WI) to construct plasmid pPH118. pPH118 was digested with *StuI* and the 3210 bp vector fragment gel purified and religated to construct plasmid pPH119 which lacks the duplicated 10 bp sequence CGAGGCCTCG (SEQ ID NO:17) (*StuI* site underlined) that was found by sequence analysis to be present in plasmid pC8. Elimination of the 10 bp *StuI/StuI* fragment in pPH119 was verified by sequencing using universal M13 forward and reverse primers.

The paragraph bridging pages 53 and 54 has been amended as follows (text that has been added is double-underlined to differentiate it from the originally underlined text):

Example C3: Construction of a plastid-targeted bacteriophage T7 RNA polymerase gene fused to the tobacco PR-1a promoter

A synthetic oligonucleotide linker comprising an *NcoI* restriction site and ATG start codon followed by the first seven plastid transit peptide codons from the *rbcS* gene (encoding the small subunit of ribulose biphosphate carboxylase) and endogenous *PstI* restriction site (top strand: 5'-CAT GGC TTC CTC AGT TCT TTC CTC TGC A-3' (SEQ ID NO:18); bottom strand: 5'-GAG GAA AGA ACT GAG GAA GC-3' (SEQ ID NO:19)), a 2.8 kb *PstI/SacI* DNA fragment of pCGN4205 (McBride, K. E. et al. (1994) PNAS 91, 7301-7305) containing the bacteriophage T7 RNA polymerase gene (T7 Pol) fused in frame to the 3' portion of the *rbcS* gene transit peptide coding sequence, a 0.9 kb *NcoI/KpnI* DNA fragment of pCIB296 containing

the tobacco PR-1a promoter with an introduced *NcoI* restriction site at the start codon (Uknes et al. (1993) Plant Cell 5, 159 169) and 4.9 kb *SfiI/KpnI* and 6.6 kb *SacI/SfiI* fragments of binary Agrobacterium transformation vector pSGCGC1 (a derivative of pGPTV-Hyg containing the polylinker from pGEM4 (Promega, Madison WI) cloned into the *SacI/HindIII* sites) were ligated to construct pPH110.

### **In the Claims**

Claims 11 and 24-29 have been cancelled without prejudice or disclaimer.

Claim 30 has been added.

Please amend the claims as follows:

6. (Twice Amended) A transgenic plant [which expresses] comprising a nucleic acid encoding a cellulase.

7. (Twice Amended) The plant of claim [6 comprising a heterologous DNA sequence coding for a cellulase] 6, wherein said nucleic acid is stably integrated into [its] a nuclear or plastid [DNA] genome of the plant and is under control of a promoter active in plants.

9. (Amended) The plant according to claim 8 wherein [the] said chemically-inducible [inducible] promoter is [PR-1] one of a PR-1, PR-1a, PR-2, PR-3, PR-4, and PR-5 promoter.

12. (Amended) The plant according to claim 6, wherein [the cellulose-degrading enzyme] said cellulase is of non-plant origin.

13. (Amended) The plant according to claim 6, wherein [the cellulose-degrading enzyme is of microbial origin, preferably of bacterial origin] said cellulase derives from a microorganism.

14. (Amended) The plant according to claim [13] 30, wherein [the cellulose-degrading enzyme is from a] said bacterium [of the genus] is a *Thermomonospora* bacterium.

15. (Amended) The plant according to claim 14, wherein [the cellulose-degrading enzyme is from] said bacterium is *T. fusca*.

18. (Amended) The plant of claim 6, wherein [the] said cellulase is an endocellulase [( $\beta$ -1,4-endoglucanase or  $\beta$ -D-glucosidase)].

19. (Amended) The plant of claim 7 wherein [the heterologous DNA sequence further comprises] said nucleic acid further encodes a targeting sequence.

20. (Amended) The plant of claim 19 wherein [the] said targeting sequence [is] comprises a vacuole-targeting sequence.

22. (Amended) A transgenic seed obtained from the plant of claim 6.

23. (Amended) A transgenic seed obtained from the plant of claim 7 wherein [said] the seed comprises [the heterologous DNA sequence] said nucleic acid.